Exhibit I

NEW ENGLAND COMPOUNDING CENTER

MASTER SOP LIST	
1.010	Policies and Procedures
1.030	Deviations - OOS
1.040	Log of Maintenance and Cleaning (L-MAC)
1.050	General Non-Sterile Compounding Technique
1.060	General Aseptic Technique
2.010	Employee Orientation/Training
2.020	Compounding Personnel Orientation Program
2.030	Sterile Compounding Personnel Qualifications/Training
2.040	Non-Sterile Compounding Personnel Qualification
3.010	Sterile Compounding Area Requirements
3.020	Cleaning and Maintenance of the Clean Room Facility
3.030	Environmental Monitoring of the Clean Room Facility
3.040	Non-Sterile Compounding Area Requirements
3.050	Cleaning and Maintenance of the Non-Sterile Compounding Area
3.060	Cleaning and Maintenance of Clean Room 2 Facility
4.010	Compounding Equipment
4.020	Use, Calibration and Maintenance of the Drug Product Refrigerator and Freezer
4.030	Use, Calibration and Maintenance of the Analytical Balances
4.050	Use, Verification and Maintenance of the Dry-Heat Oven
4.060	Use, Verification and Maintenance of the Autoclave
4.070	Use, Calibration and Maintenance of the Incubator
4.090	Use, and Maintenance of the Exakt Three Roll Ointment Mill
4.100	Use, Calibration and Maintenance of the Baxa Repeater Pump
4.110	Use, and Maintenance of the Capsule Machine
4.111	Use, and Maintenance of the Anprolene Gas Sterilizer
5.010	Out Patient Medication Records System
5.020	Outpatient Prescription Processing: Counseling, HIPPA and Complaints
5.030	Customer Complaint Handling
5.050	Delivery of Compounded Preparations
5.070	Controlled Substances CIII to V Inventory
5.080	Controlled Substances CII
6.010	Product Procurement, Receipt and Inspection
6.020	Product Labeling
7.010	Handling of Cytotoxic Drug Compounds
7.020	Disposing of Cytotoxic Drug Waste
7.030	Cytotoxic Drug Spills

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NEW ENGLAND COMPOUNDING CENTER

8.010	Sterilization and Depyrogenation
9.010	The Quality Assurance Program
9.020	Good Documentation Practices (GDP)
9.030	Corrective and Preventative Action (CAPA) Management
9.040	Formula Worksheet – The Compounder RX
9.050	Beyond - Use Dating (BUD) of Compounded Preparations
9.060	Product Quarantine, Storage, Release and Disposal
9.070	Recall of Compounded Product
9.080	Operation and Maintenance of Meritech Cleantech 2000S Hand Washers
9.090	Required Garb for Clean Room Facility Access
9.100	Sterile Compounding Process Validation (MEDIA FILLS)
9.110	Sterile Compounding Finished Preparation Testing
9.120	Required Garb for Non-Sterile Compounding Area
9.130	Non-Sterile Compounding Process Validation
9.140	Non-Sterile Compounding Finished Preparation Testing

NEC002197

TITLE: STERILE COMPOUNDING AREA REQUIREMENTS		
SOP NUMBER: 3.010	VERSION NUMBER: 2.0	
Sterile Laboratory	Effective Date	03-11-08
Originator:		
Reviewer:		

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements for compounding in a sterile environment.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center clean room facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>.

2.2 This procedure must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure or document that another staff member has been designated to complete this task.

3.2 The Pharmacist-in-charge shall be responsible for ensuring that only trained personnel are allowed to work in the sterile compounding area. No other personnel or patients will be allowed within the sterile compounding area.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.3 SOP 3.030 "Environmental Monitoring of the Clean Room Facility"

5.0 DEFINITIONS

5.1 Clean Room – Area with limited access that is designated for compounding and packaging of compounded sterile preparations (CSPs) and is engineered to meet or exceed Class 1000 (ISO Class 6) standards.

5.2 Gown Room – Area adjacent to the clean room that reduces traffic around the clean room doors and is engineered to meet or exceed Class 10,000 (ISO Class 7) standards.

5.3 Glove Box – Provides no less than a Class 10 (ISO Class 4) working environment for sterile compounding.

5.4 Environmental Monitoring (EM) – Sampling of air and surfaces in critical sites (glove boxes, clean room, crimp room, gown room) in order to confirm compliance with performance objectives and to detect contamination.

6.0 FREQUENCY

6.1 Every 6 months, Class 10 (ISO Class 4), or less, areas shall be re-qualified (glove boxes).

6.2 Every 6 months, Class 1000 (ISO Class 6), or greater, areas shall be re-qualified, and air pressure difference shall be verified (clean room).

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NEC002267

TITLE: STERILE COMPOUNDING AREA REQUIREMENTS

SOP NUMBER: 3.010 **VERSION NUMBER: 2.0**

7.0 EQUIPMENT & SUPPLIES

7.1 N/A

8.0 GENERAL INFORMATION

8.1 The air-handling system in the clean room is engineered to provide positive pressure using HEPA filters that reduce particulate matter in order to meet or exceed Class 1000 (ISO Class 6) standards.

9.0 PROCEDURE

9.1 An appropriate clean room shall be used for sterile compounding according to USP <797> guidelines.

9.2 In order to produce a sterile environment in the clean room, the air handling system must create positive pressure (in relation to the anteroom) within the clean room. This environment shall be Class 1000 (ISO Class 6) and shall contain a Class 10 (ISO Class 4) glove box.

9.3 The gown room must provide controlled access to the clean room and must meet or exceed Class 10,000 (ISO Class 7) standards. The gown room must have positive pressure in relation to the outside environment and should have negative pressure in relation to the clean room.

9.4 All surfaces (ceilings, walls, floors, fixtures, shelving, counters, cabinets, etc.) in the clean room must be smooth, impervious, non-shedding and free from cracks and crevices.

9.5 No one may enter the clean room unless appropriate garb is worn.

9.6 Only cleaned and sanitized furniture, equipment, supplies and other goods required for sterile compounding may be brought into any area of the clean room and must be non-permeable, non-shedding and chemically resistant to disinfectants.

9.7 Equipment and similar items used in the clean room shall not be removed from the room except for calibration, servicing or proper maintenance. If equipment or similar items are removed from the clean room, they must be properly cleaned and disinfected before reentering the clean room.

9.8 Clean room cleaning supplies (mops, etc.) shall be designated for use only in the clean room. Cleaning must be performed as per SOP 3.020, "Cleaning and Maintenance of the Clean Room Facility."

9.9 An EM program shall be established, documented and implemented as per SOP 3.030, "Environmental Monitoring of the Clean Room Facility."

10.0 ATTACHMENTS

10.1 N/A

11.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP	CR06010
2.0	03-11-08	Changed buffer to clean, other minor changes	CR08008

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NEC002268

TITLE: CLEANING AND MAINTENANCE OF THE CLEAN ROOM FACILITY		
SOP NUMBER: 3.020	VERSION NUMBER: 9.0	
Sterile Laboratory	Effective Date	06/22/11
Originator:		
Reviewer:		

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements and documentation for cleaning and maintenance of the clean room facility.

2.0 SCOPE

2.1 This procedure applies to the New England Compounding Center facility under conditions that meet or exceed state and federal guidelines as outlined by the United States Pharmacopeia <797>. This policy must be followed to reduce the amount of particulate matter and airborne microbial contamination.

3.0 RESPONSIBILITY

3.1 Quality Control shall supervise this procedure and document that all personnel responsible for cleaning and maintenance of the clean room facility shall comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 SOP 1.060 "General Aseptic Technique"

4.3 SOP 3.030 "Environmental Monitoring of the Clean Room Facility"

4.4 SOP 9.090 "Required Garb for Clean Room Facility Access"

5.0 DEFINITIONS

5.1 N/A

6.0 FREQUENCY

6.1 Cleaning shall be performed as described in this procedure on a daily, weekly and monthly basis.

7.0 EQUIPMENT & SUPPLIES

7.1 Mop with exchangeable mop-head

7.2 Tacky mat

7.3 Lint-free towels or wipes

7.4 Distilled or Purified Water

7.5 2% bleach solution (prepared with 80ml bleach and 1 gallon of distilled water)

7.6 LpH - 1oz (30ml) added to 2 gallons of distilled water

7.7 Vesphene - 2oz (59ml) added to 2 gallons of distilled water

7.8 70% Sterile Isopropyl Alcohol (IPA)

7.9 Sporicide (Sporicidin, Spor-Klenz, or anti-spore solution)

7.10 Waste container liners

7.11 Step stool

7.12 Room thermometer

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7.11 Room hygrometer

8.0 GENERAL INFORMATION

8.1 Cleaning Solutions

8.1.1 Rotation of disinfectants is performed to suppress populations of different types of organisms which may be inherently resistant to one or another type of disinfectant.

8.1.2 LpH and Vesphene, while broad based disinfectants, will be rotated as each has a different pH range which may target different types of organisms. ***(7 day expiration).***

8.1.3 A sporicide will be rotated to suppress spore forming bacteria or mold which is inherently resistant to primary or secondary disinfectants.

8.1.4 Clean floor with 2% bleach solution - to be prepared as needed ***(4 hour expiration).***

8.1.5 Sterile 70% IPA - for use in areas with equipment that may be damaged by the use of bleach. **All IPA designated for use in the clean room facility must be sterile.**

8.2 All primary disinfectants and sporicidal agents require a minimum wet contact time of ten (10) minutes with the surface to which it was applied.

9.0 PROCEDURE

9.1 Follow all applicable SOPs for gowning and transport of materials into the Clean Room Areas.

9.2 Daily- (AM)

9.2.1 Refresh tacky mat.

9.2.2 Clean/sanitize Hoods 1, 2, 3, 4 and 5; Chemo Hood; Horizontal Hoods 1, 2A, 2B, 2C; Glove boxes and Antechambers with sterile 70% IPA.

9.2.3 Clean/sanitize Stations 1, 2, 3, and 4; Tables 1, 2, 3, 4, 5 and 6; including carts, with sterile 70% IPA.

9.2.4 Clean/sanitize balances, hot /stir plates, weigh hoods, computer stations 1 & 2, and telephones, with sterile 70% IPA.

9.2.5 Clean/sanitize sink with Spor-klenz.

9.2.6 Clean/sanitize chairs with sterile 70% IPA.

9.2.7 Document all cleaning on the appropriate attachment.

9.3 During Day

9.3.1 Refresh tacky mat.

9.3.2 Clean/sanitize Hoods 1, 2, 3, 4 and 5; Chemo Hood; Horizontal Hoods 1, 2A, 2B, 2C; Glove boxes and Antechambers with sterile 70% IPA.

9.3.3 Clean/sanitize Stations 1, 2, 3, and 4; Tables 1, 2, 3, 4, 5 and 6; including carts, with sterile 70% IPA.

9.3.4 Clean/sanitize pass-thru, with Spor-klenz or sterile 70% IPA.

9.3.5 Document all cleaning on the appropriate attachment.

9.4 Daily (PM)

9.4.1 Clean/sanitize Stations 1, 2, 3, and 4; Tables 1, 2, 3, 4, 5 and 6, with Spor-klenz or Sporicidin. Allow to set for at least 10 minutes, disperse with lint-free towels and allow to set overnight.

9.4.2 Clean/sanitize Hood s 1, 2, 3, 4 and 5; Chemo Hood; Horizontal Hoods 1, 2A, 2B, 2C glove boxes and antechambers with Spor-klenz or Sporicidin. Allow to set for at least 10 minutes, disperse with lint-free towels and allow to set overnight.

9.4.3 Clean/sanitize Sink with Spor-klenz or Sporicidin. Allow to set for at least 10 minutes and to set overnight.

9.4.4 Change mop head.

9.4.5 Empty Trash

9.4.4 Mop floors with 2% bleach solution 1 week, alternating with LpH 1 week (Jan → June), rotating with Vesphene (July → Dec).

9.4.6 When using Bleach on metal/stainless steel surfaces, follow with sterile 70% IPA

9.4.6 Document all cleaning on the appropriate attachment.

9.5 Weekly

9.5.1 Clean/sanitize all waste receptacles with Spor-klenz or Sporicidin.

9.5.2 Clean/sanitize entire gown room rotating Spor-klenz and LpH (Jan→June), then spork-lenz and Vesphene (July→Dec).

9.5.3 Clean Autoclave "IN".

9.5.4 Clean Autoclave "OUT".

9.5.5 Document all cleaning on attachment.

9.6 Bi-Weekly

9.6.1 Hepa Vacuum All Rooms (clean room, middle room, gown room).

9.7 Monthly

9.7.1 Clean walls and ceilings. Outside Vendor - **UniClean/Contamination Control Services.**

9.7.2 Clean/sanitize refrigerators/freezers with 70% IPA (sterile).

9.7.3 Clean/sanitize Hood 1 with Spor-Klenz

9.7.4 Clean/sanitize Hood 2 with Spor-Klenz.

9.7.5 Clean/sanitize Hood 3 with Spor-Klenz

9.7.6 Clean/sanitize Hood 4 with Spor-Klenz.

9.7.7 Clean/sanitize Hood 5 with Spor-Klenz

9.7.8 Clean/sanitize Chemo Hood with Spor-Klenz

9.7.9 Clean/sanitize Horizontal 1 Hood with Spor-Klenz

9.7.10 Clean/sanitize Horizontal 2A Hood with Spor-Klenz

9.7.11 Clean/sanitize Horizontal 2B Hood with Spor-Klenz

9.7.12 Clean/sanitize Horizontal 2C Hood with Spor-Klenz

9.7.13 Clean/sanitize Station 1 with Spor-Klenz.

9.7.14 Clean/sanitize Station 2 with Spor-Klenz.

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9.7.15 Clean/sanitize Station 3 with Spor-Klenz.

9.7.16 Clean/sanitize Station 4 with Spor-Klenz.

9.7.17 Clean/sanitize Computer Stations 1 & 2.

9.7.18 Clean/sanitize Alcohol Table with Spor-Klenz.

9.7.19 Clean/sanitize Beaker Shelves with Spor-Klenz.

9.7.20 Clean/sanitize Cap Shelves with Spor-Klenz.

9.7.21 Clean/sanitize Crimp Station with sterile 70% IPA or Spor-Klenz.

9.7.22 Clean/sanitize Luer to Luer /Tamper Evident Cap Shelves with 70% sterile IPA or Spor-Klenz.

9.7.23 Clean/sanitize Nalgene Shelves with 70% sterile IPA or Spor-Klenz.

9.7.24 Clean/sanitize Refrigerators with 70% sterile IPA or Spor-Klenz.

9.7.25 Clean/sanitize Freezers with 70% sterile IPA or Spor-Klenz.

9.7.26 Clean/sanitize Sink Station with 70% sterile IPA or Spor-Klenz.

9.7.27 Clean/sanitize Sterile Cup/Eye Drop Shelves with 70% sterile IPA or Spor-Klenz.

9.7.28 Clean/sanitize Stopper shelves with 70% sterile IPA or Spor-Klenz.

9.7.29 Clean/sanitize Syringe Shelves with 70% sterile IPA or Spor-Klenz.

9.7.30 Clean/sanitize Under Sink with 70% sterile IPA or Spor-Klenz.

9.7.31 Clean/sanitize Drug Shelves 1 with 70% sterile IPA or Spor-Klenz.

9.7.32 Clean/sanitize Drug Shelves 2 with 70% sterile IPA or Spor-Klenz.

9.7.33 Clean/sanitize Drug Shelves 3 with 70% sterile IPA or Spor-Klenz.

9.7.34 Clean/sanitize Drug Shelves 4 with 70% sterile IPA or Spor-Klenz.

9.7.35 Clean/sanitize Drug Shelves 5 with 70% sterile IPA or Spor-Klenz.

9.7.36 Clean/sanitize Drug Shelves 6 with 70% sterile IPA or Spor-Klenz.

9.7.37 Clean/sanitize Miscellaneous Shelves with 70% sterile IPA or Spor-Klenz.

9.7.38 Clean/sanitize Sterile IV Bags Etc...Shelves with Spor-klenz or 70% sterile IPA.

9.7.39 Clean/sanitize Sodium Chloride Bottle Shelves with 70% sterile IPA or Spor-Klenz.

9.7.40 Clean/sanitize Vial Shelves with 70% sterile IPA or Spor-Klenz.

9.7.41 Biannual-Cleaning/Maintenance/Filter changes

9.7.42 Clean/sanitize Hand washer with Spor-klenz or 70% sterile IPA (included in weekly cleaning of the entire gown room).

9.7.43 Change Sterile IPA bottles every six months (May & November).

9.7.44 Change pre-filters on hoods (July)

9.7.45 Clean/sanitize Auto Crimper and hand Crimpers with 70% sterile IPA.

~~9.7.46 Document all cleaning on the appropriate attachment.~~

9.8 Annual Maintenance

9.8.1 Meritech Hand washer Vendor

9.8.1.1 Twice a year maintenance.

9.9 The necessary cleaning materials are dedicated solely to cleaning the clean room facility. These materials shall be stored in the preparation room of the clean room facility and shall be kept separate from other cleaning materials.

9.10 Cleaning solutions shall be prepared as needed.

9.10.1 Do not combine disinfectants or use them in concentrations other than those outlined in the SOPs.

9.11 Cleaning Solution Preparation

9.11.1 Use only the following approved disinfectants/sporicidal agents. Adjust volumes based on the desired final volume.

- Primary Disinfectants -
  - LpH -1oz (30ml) added to 2 gallons of distilled water.
  - Vesphene - 2oz (59ml) added to 2 gallons of distilled water.
  - Assign a 7 day expiration date from preparation or the manufacturer's expiration, which ever is shorter.
- Secondary Disinfectants
  - Sterile 70% Isopropyl Alcohol (IPA) - purchase as sterile or filter through 0.22um filter.
- Sporicidal Agent
  - 2% bleach (v/v) - 80ml added to 1 gallon of distilled water.(expiration date of 4 hours)
  - Spor-klenz (ready to use) - No preparation required
  - Sporicidin – Disinfectant Towellettes
- Label the solution container with the following information.
  - Solution description
  - Expiration date

9.12 Bucket less Mop System

9.12.1 Dispense the desired solution into the mop's solution tank.

9.12.2 Saturate the mop head by pressing the flow control button.

9.12.3 The mop should leave the surface wet with out pooling.

9.12.4 When mopping, mop in one direction with overlapping strokes.

9.12.5 If solution in apply bucket becomes visibly dirty, change solution.

9.12.6 Refill solution tank when needed.

9.12.7 Discard solution in tank and rinse when cleaning is complete.

9.13 Cleaning solutions shall be prepared as needed.

9.14 Distribute solutions into individual spray bottles for use if needed and label them with the name of the disinfectant.

9.15 Refill bottles with additional disinfectant solution as necessary.

9.16 All disinfectants solutions (stock or solution spray bottles) shall be discarded at the end of every week to ensure that expired solution is not used and that containers are cleaned.

9.17 Cleaning shall be performed using a detergent followed by sanitization if there are any visible particulates. A damp, non-shedding sponge mop shall be used for cleaning.

9.18 Except for sanitization of the glove box, cleaning of the sterile compounding area is prohibited during compounding operations.

9.18.1 Ensure all compounding operations are completed and all equipment has been removed from the glove box prior to sanitization.

9.18.2 The operator must clean and sanitize the exposed work surfaces (counters and walls) of the glove box immediately before and after each batch preparation and immediately should a spill occur.

9.19 Temperature and humidity readings shall be taken in all areas of the clean room facility.

9.19.1.1 The temperature and humidity in the clean room facility shall be monitored electronically, printed out and placed in a designated binder.

9.19.1.2 The humidity should be maintained in the range of 30% - 50%.

9.19.1.3 The temperature shall be maintained between 60°F- 70°F.

9.19.2 Remove all components (equipment, bottles, adapter caps, filters, syringes, vials, etc.) from the antechambers only. Clean and sanitize with Spor-Klenz at end of day.

9.20 Weekly Requirements

9.20.1 Clean Room includes all requirements listed in section 9.5.

9.20.2 Clean and sanitize gown room and document on the appropriate attachment.

9.20.3 Allow all rooms and equipment to air dry before sterile compounding resumes.

9.20.4 Document all activities on the appropriate Cleaning and Maintenance of the Clean Room Facility forms on Attachments 1, 2 and/or 3. If the equipment is not in use, write "N/A" in the appropriate location on the form.

9.21 Monthly Requirements

9.21.1 Includes all requirements listed in section 9.7.

9.22 The Quality Manager shall ensure the completion of tasks on a daily basis and shall review and sign/date Attachments 1, 2 and 3 at the end of each month. The form shall be retained in the environmental testing binder.

10.0 ATTACHMENTS

10.1 Attachment 1 - Cleaning and Maintenance of the Clean Room - Daily(AM) and **During Day** and Daily(PM)

10.2 Attachment 2 - Cleaning and Maintenance of the Clean Room – Weekly and Monthly

10.3 Attachment 3 – Cleaning and Maintenance of the Clean Room - Monthly

11.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP	CR06011
2.0	04-04-06	Updated section 9.8.4 to include the removal and proper storage of components and equipment from the glove box before daily cleaning.	CR06057
3.0	04-20-06	Modified Attachment 1 for Clean Room 1 Facility. Added Attachment 2 for Clean Room 2 Facility. Updated overall cleaning procedure.	CR06063
4.0	N/A	Added attachment 4	N/A
5.0	11-30-07	Added weekly and monthly duties on separate attachments. Updated changes.	CR07023
6.0	01-24-08	Changes in attachment 2. Needed to specify what was being cleaned.	CR08002
7.0	12/22/08	Updated cleaning and maintenance to fit schedule in clean room	CR08018
8.0	08/31/09	Changed attachments to match equipment.	CR09001
9.0	06/30/11	Updated Changes to match new Clean Room Facility, added a new cleaning attachment, deleted temperature and humidity attachment.	CR11003

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TITLE: STERILE COMPOUNDING PROCESS VALIDATION (MEDIA FILLS)	
SOP NUMBER: 9.100	VERSION NUMBER: 2.0
Sterile Laboratory	First effective Date: 02-08-06
Originator: Cynthia M. Robinson	Previous Effective Date: 03-08-06
Reviewer: Barry	Current Effective Date: 02-28-08

PURPOSE

1.1 The purpose of this procedure is to establish requirements for sterile compounding process validations (media fills) in accordance with USP <797>.

2.0 SCOPE

2.1 This procedure applies to all sterile compounding personnel at New England Compounding Center.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all sterile compounding personnel will comply with this procedure.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 SOP 2.030 "Sterile Compounding Personnel Qualification"

4.3 SOP 3.020 "Cleaning and Maintenance of the Clean Room Facility"

4.4 SOP 3.030 "Environmental Monitoring of the Clean Room Facility"

5.0 DEFINITIONS

5.1 Aseptic Filling – process in which a pre-sterilized product is transferred to a sterile container(s)

5.2 Aseptic Processing – the aseptic filling of product containers and/or devices in a controlled environment where the air supply, materials, equipment and personnel are regulated to control microbial and particulate contamination to acceptable levels

5.3 Aseptic Processing Area – controlled environment for sterile compounding; consists of several zones in which the air supply, materials, equipment and personnel are regulated to control microbial and particulate contamination to acceptable levels

5.4 Critical Processing Zone – region of aseptic processing area in which product and contact surfaces are exposed to the environment

5.5 Media Fill – method of evaluating an aseptic process using a microbial growth medium

5.6 CSP – Compounded Sterile Preparation

6.0 FREQUENCY

6.1 High-Risk Level – each person at least semi-annually

7.0 EQUIPMENT & SUPPLIES

7.1 ISO Class 4 (Class 10) microenvironment

7.2 See" Compounder " for Media Fill (Personal) 3% Injection

7.3 Each aseptic employee must perform 3 consecutive media fills runs without evidence of turbidity< (-) control> prior to working with sterile medications/formulations.

7.4 3GMS Soybean-Casein Digest Medium Powder
7.5 100 ML Sterile water for injection
7.6 Sterile weigh-cup
7.7 (3) 35 ML LL Sterile syringes
7.8 (18) Sterile 10mL clear vials (1) for Control, (5) for sterile
7.9 (3) 0.22M Disk filters
7.10 (3) 18G LL needles
7.11 (3) Red LL syringe caps
7.12 Flip-Top Caps
7.13 (18) 20MM stoppers...3 for Controls are **non sterile**
7.14 Sterile 70% isopropyl alcohol (IPA) or disinfectant in use
7.15 Sterile Rubber Closures
7.16 Incubator
7.17 (4) TSA contact plates

8.0 GENERAL INFORMATION

8.1 Media fills must be conducted without interruption.
8.2 Media fills shall be performed under the most challenging or stressful conditions encountered during compounding.

9.0 PROCEDURE

9.1 Media Fill Procedures

9.1.1 Verification of growth promotion of media may be done concurrently with the media fill and verified after the media fill run (certificate of analysis indicating vendor Growth Promotion is acceptable).

9.1.1.1 The incubation temperature will be the same as that used for the media filled units.

9.1.1.2 The medium selected must be capable of growing a wide spectrum of microorganisms and of supporting microbiological recovery and growth of low numbers of microorganisms.

9.1.2 High-Risk Media Fills

9.1.2.1 All media fills shall be conducted using the current compounder records.

9.1.2.2 All critical steps must occur in an ISO Class 4 (Class 10) microenvironment.

9.1.2.3 Disinfect the glove box in accordance with SOP 3.020, "Cleaning and Maintenance of the Clean Room Facility."

9.1.2.4 Components should be assembled and brought into the sterile area in a clean tote or equivalent.

9.1.2.5 Disinfect each component prior to placing in the glove box.

9.1.2.6 Weigh using an electronic analytical balance, 3g of Soybean-Casein Digest Medium in a sterile weigh cup to make a 3% solution. Print weight and attach to log sheet.

9.1.2.7 Add 80% of final volume of sterile water for injection to sterile cup. Add spin bar and cover.

9.1.2.8 Spin until completely dissolved. QS to final volume.

9.1.2.9 Draw 30mL of above solution into (3) separate 35ML lure lock syringes via 18 gauge needle then cap syringes.

9.1.2.10 Outside class-10 hood transfer 5mL of the solution from each syringe into separate sterile 10mL clear vials.

9.1.2.11 The above 3 vials are to be treated and labeled as **controls** they generate exponential microbial growth, indicated by visible turbidity upon incubation.

9.1.2.12 Using proper aseptic technique transfer the 3 syringes and all other necessary materials containing 25ML of 3% soybean solution into the class-10 microenvironment.

9.1.2.13 Attach a sterile 0.2M disk and an 18 gauge needle to each syringe and filter 5ML of the 3%TSB solution into each of the (5) x 10ML clear vials...Repeat process for each syringe.

9.1.2.14 Cap, crimp and label each vial.

9.1.2.15 Incubate vials for 14 days at 25-35 °C and check for turbidity at 14 days.

9.2 Incubation and Inspection of Media-Filled Units

9.2.1 Leaking or damaged media fill units must be removed, and documented why the reason for removal.

9.2.2 All media fill units shall be incubated for 14 days at 25-35°C.

9.2.3 All media fill units shall be stored or manipulated to allow contact of the media with all product contact surfaces in the unit.

9.2.4 At the end of 3, 7 and 14 day incubation period, each media fill unit shall be visually inspected for the presence of microbial growth.

9.2.5 Media must be transferred into a clear glass container if the container is not suitable for visual inspection.

9.3 Contamination with Media

9.3.1 Contamination of the area and equipment with media during media-fill runs shall not compromise the quality of the facility and equipment or the product subsequently processed using the same facility and equipment.

9.3.2 Media spills must be handled properly and promptly by cleaning, disinfecting and, if necessary, sterilizing the facility and equipment.

9.4 Documentation Requirements for Media Fills

9.4.1 The Validation of Personnel – Sterile Compounding form (Attachment 2 of SOP 2.030, "Sterile Compounding Personnel Qualification") shall include, but not be limited to, the following items:

9.4.1.1 Date and location of media fill

9.4.1.2 Container/closure descriptions (type, lot number and size)

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9.4.1.3 Volume filled

9.4.1.4 Filter brand/description and lot numbers/expiration date (if applicable)

9.4.1.5 Type of media used, lot number/expiration date and growth promotion date/results (if purchased, a certificate of growth promotion should be maintained on file)d

9.4.1.6 Number of units rejected at inspection and reason for rejection

9.4.1.7 Number of units incubated and incubation time/temperature

9.4.1.8 Number of positive units at the conclusion of the incubation

9.4.1.9 Results (pass/fail)

9.4.2 Touch Plates

9.4.2.1.1 The compounder shall take two samples of his or her dominant hand to monitor aseptic technique. **Prior to disinfecting gloves**, the compounder shall touch each gloved fingertip to the agar surface, making certain to not re-touch areas.

9.4.2.1.2 Gloves must be disinfected prior to continuing the media fill after touching the agar surface.

9.4.2.2 Disinfect each sampled surface immediately after the sample is taken with sterile 70% IPA.

9.4.2.3 There shall be one positive control contact plate for each lot of media used. Touch the agar surface with an un-gloved fingertip, replace the lid, label the plate appropriately and incubate according to step 9.2.2.

9.4.2.4 There shall be one negative control contact plate for each lot of media used. Label an unopened plate appropriately and incubate according to step 9.2.2.

9.4.3 Incubation of Environmental Controls and Samples

9.4.3.1 All plates shall be incubated at 20 - 25°C for three days and then incubated at 30-35°C for three days.

9.4.3.2 Plates should be checked daily for growth.

9.5 Acceptance Criteria

9.5.1 All media must demonstrate growth promotion capabilities

9.5.1.1 If no growth is observed in the growth promoting containers, repeat the growth promotion study with new components. Incubate the samples at 30-35°C with a negative control for seven days or until growth is observed. If no growth is observed, the medium is unacceptable for use, and the results of the media fill are invalid.

9.5.1.2 A Certificate of Analysis indicating vendor growth promotion is acceptable.

9.5.2 Calibration documentation of all equipment must be current and verified.

9.5.3 The clean room temperature must be maintained at 60°F – 70°F.

9.5.4 The clean room humidity must be maintained in the 15% – 60%.

10.0 ATTACHMENTS

N/A

11.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP	CR06045
2.0	02-28-08	Took out attachment 1, section 9.1.2, 9.1.3, 9.5 changes to sections 9.5.2.2, 9.5.3, 9.6 and other changes and updates.	CR08004

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NEC002463

TITLE: STERILE COMPOUNDING FINISHED PREPARATION TESTING		
SOP NUMBER: 9.110	VERSION NUMBER: 2.0	
Sterile Laboratory	First Effective Date	02-08-06
Originator:	Previous Effective Date	03-08-06
Reviewer:	Current Effective Date	02-28-08

1.0 PURPOSE

1.1 The purpose of this procedure is to establish requirements and documentation for finished preparation testing of sterile compounded preparations.

2.0 SCOPE

2.1 This procedure applies to all sterile compounding personnel at New England Compounding Center.

3.0 RESPONSIBILITY

3.1 The Pharmacist-in-charge shall supervise this procedure and document that all sterile compounding personnel responsible for finished preparation testing comply with this procedure.

3.2 It is the responsibility of New England Compounding Center to review and assess the contract laboratory for appropriate regulatory compliance.

4.0 REFERENCES

4.1 USP Current Version <797> "Pharmaceutical Compounding – Sterile Preparations"

4.2 USP Current Version <71> "Sterility Testing"

4.3 USP Current Version <85> "Bacterial Endotoxin Testing"

4.4 USP Current Version <1075> "Good Compounding Practices"

4.5 All Mass State Board requirements

4.6 SOP 6.020 "Product Labeling"

4.7 SOP 9.050 "Beyond-Use Dating (BUD) of Compounded Preparations"

4.8 SOP 9.060 "Product Quarantine, Storage and Release"

4.9 SOP 9.070 "Recall of Compounded Product"

5.0 DEFINITIONS

5.1 CSP – Compounded Sterile Preparation

6.0 FREQUENCY

6.1 Testing requirements are dependent on USP monographs for each compound. It is the responsibility of New England Compounding Center to determine which tests can be performed in-house and which tests must be performed at a contract facility.

7.0 EQUIPMENT & SUPPLIES

7.1 Third party analytical testing laboratory (if applicable)

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7.2 Lint-free wipes

7.3 Powder-free latex or nitrile gloves

8.0 GENERAL INFORMATION

8.1 This procedure is designed for planned testing to verify and demonstrate effectiveness of all procedures critical to the accuracy and purity of the finished compounded product.

8.2 All compounded sterile products must be tested according to USP <797> and other referenced chapters and monographs.

8.2.1 USP <71> must be followed when a sterility test is required. Within chapter <71>, the number of units, volume per unit and specific methods are discussed.

8.2.2 USP <71> states, "The following culture media have been found to be suitable for the test for sterility. Fluid Thioglycollate Medium is primarily intended for the culture of anaerobic bacteria. However, it will also detect aerobic bacteria. Soybean-Casein Digest Medium is suitable for the culture of both fungi and aerobic bacteria."

9.0 PROCEDURE

9.1 Sterility Testing

9.1.1 Low-risk level preparations shall be tested for sterility:

9.1.1.1 Before administration.

9.1.1.2 If stored at room temperature for more than 48 hours.

9.1.1.3 If stored at 2°C - 8°C for more than 14 days.

9.1.1.4 If stored at frozen conditions (less than -20°C) for more than 45 days.

9.1.2 Medium-risk level preparations shall be tested for sterility:

9.1.2.1 Before administration.

9.1.2.2 If stored at room temperature for more that 30 hours.

9.1.2.3 If stored at 2°C - 8°C for more than 7 days.

9.1.2.4 If stored at frozen conditions (less than -20°C) for more than 45 days.

9.1.3 High-risk level preparations shall be tested for sterility:

9.1.3.1 Before administration.

9.1.3.2 If stored at room temperature for more than 24 hours.

9.1.3.3 If stored at 2°C - 8°C for more than 3 days.

9.1.3.4 If stored at frozen conditions (less than -20°C) for more than 45 days.

9.1.3.5 If drug(s) that will be injected into vascular and/or central nervous systems is/are prepared in groups of more than 25 identical, individual single-dose packages, or in multiple dose vials for administration to multiple patients.

9.1.3.6 If, prior to sterilization, drug(s) that will be injected into vascular and/or central nervous systems is/are stored at 2°C - 8°C for more than 12 hours or stored at temperatures above 8°C for more than 6 hours.

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9.1.4 Sterility sampling requirements must follow the tables in USP <71>, "Sterility Testing."

9.1.5 Sterility methods must follow the USP <71> membrane filtration method (if applicable). If not performing membrane filtration, other methods outlined in USP <71> are acceptable.

9.1.6 If a rapid sterility test is used, it must be proven that the method is as effective and as reliable as the USP method(s).

9.2 Endotoxin (Pyrogen) Testing

9.2.1 High-risk level preparations:

9.2.1.1 CSPs for administration via injection into the vascular and central nervous systems that are prepared in groups of more than 25 identical individual single-dose packages, or in multiple dose vials for administration to multiple patients, must not contain excessive bacterial endotoxins.

9.2.1.2 CSPs that are exposed to 2°C - 8°C for more than 12 hours or that are exposed to temperatures above 8°C for more than 6 hours before sterilization must be tested for excessive endotoxins.

9.2.2 The endotoxin testing shall follow the USP <85> bacterial endotoxin test method(s).

9.2.3 In the absence of a bacterial endotoxin limit in the official monograph or other CSP formula source, the CSP must not exceed the amount of USP Endotoxin Units (EU per hour per kg of body weight or m^2 of body surface area) specified in USP <85> for the appropriate route of administration.

9.2.4 One unit per batch must be sampled.

9.3 Physical Testing Requirements

9.3.1 The end product must be visually inspected for:

9.3.1.1 Container leaks

9.3.1.2 Integrity

9.3.1.3 Solution cloudiness or phase separation

9.3.1.4 Appropriate color

9.3.1.5 Appropriate volume

9.3.2 Particulate testing (liquids)

9.3.2.1 Sampling (one unit per batch and, if placed in storage, immediately before shipping).

9.3.2.2 Wipe the container with a damp, lint-free wipe to remove any external particles.

9.3.2.3 Using powder-free gloves, hold the container by its top and swirl the contents by rotating the wrist in a circular motion.

9.3.2.4 Hold the container horizontally about four inches below a light source against a white and/or black background and move the container back and forth.

9.3.2.5 Slowly invert the container and look for heavy particles that may have settled on the bottom of the container.

9.4 Accuracy Requirements

9.4.1 Accuracy must meet Mass State Board requirements.

9.4.2 All calculations and volumes must be verified on the formulation sheet (e.g. if the total volume shall be 5mL, then fill 5mL of water into a container of similar size/shape and visually compare).

9.5 Identification and Potency Requirements

9.5.1 Verify the label has the correct:

9.5.1.1 Names

9.5.1.2 Amounts or concentrations of ingredients

9.5.1.3 Total volume

9.5.1.4 Beyond-use date

9.5.1.5 Appropriate route(s) of administration

9.5.1.6 Storage conditions

9.5.1.7 Other safe use information as needed

9.5.2 Verify the compounding record to the original written order for correct identities of ingredients, purity of ingredients and amounts of ingredients. If any of these cannot be confirmed accurate, the preparation must be assayed by methods that are specific for the active ingredients based on USP monographs

9.5.3 Verify that correct fill volumes and quantities of units were prepared.

9.5.4 At the discretion of the Pharmacist-in-charge, samples shall be tested for potency using the appropriate method or samples shall be sent to a contract lab for testing. Samples that are awaiting potency results must be quarantined as per SOP 9.060, "Product Quarantine, Storage and Release."

9.6 If any of the finished product testing is out of specification, an investigation must be performed to determine if a product recall (SOP 9.070) is necessary.

10.0 ATTACHMENTS

10.1 Attachment 1 – Test Results Data Sheet (Sterile)

TITLE: STERILE COMPOUNDING FINISHED PREPARATION TESTING	
SOP NUMBER: 9.110	VERSION NUMBER: 2.0

11.0 HISTORY

Version Number	Date Effective	Description of Change	Change Request Number
1.0	03-08-06	New SOP	CR06046
2.0	02-28-08	Removed sections 9.4.3, 9.6 and 9.7	CR08006

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TEST RESULTS DATA SHEET (STERILE)

Product Name: _____ **Lot #:** _____

Prepared By: _____ **Date:** _____

Pharmacy testing results acceptable? ☐Yes ☐No ☐N/A

If "No," OOS/Investigation number: _____

Copy of final investigation results attached? ☐Yes ☐No (explain)

_____

_____

_____

_____

If "N/A," contract laboratory results acceptable? ☐Yes ☐No

Contract laboratory investigation results attached? ☐Yes ☐No (explain)

_____

_____

_____

_____

Contract laboratory final results attached? ☐Yes ☐No (explain)

_____

_____

_____

_____

Completed By: _____ **Date:** _____

Pharmacist-in-charge

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